



Claims

- 1. Use of ERβ-selective ligands for production of medicaments for regulating fertility with or without additional use of follicular sex steroids.
- 2. Use of ERβ-selective agonists according to claim 1 for treatment of female infertility
- 3. Use according to claim 2 to support IVF (in vitro fertilisation) in connection with in vivo treatment.
- 4. Use according to claim 2 for treatment of females which are suffering from ovarian infertility (PCO syndrom).
- 5. Use for treatment of ovarian failure associated with aging.
- 6. Use of ERβ-selective antagonists according to claim 1 for ovarian contraception.
- 7. Use according to claim 6 for inhibiting folliculogenesis.
- 8. Use according to claim 6 for inhibiting ovulation.
- 9. Use according to claim 6 to inhibit preimplantational development of ovulated oocytes.
- 10. Use of ERβ-selective ligands according to claim 1 for production of medicaments for regulating fertility without additional use of follicular sex steroids.
- 11. Use of ERβ-selective ligands according to claim 10 for production of medicaments for regulating fertility without additional use of a progestin.
- 12. 17-Chloro-D-homosteroids of general formula I

$$R_{10}$$
 R_{2}
 R_{4}
 R_{10}

(1)





in which

R₁/means a hydrogen atom or a C₁₋₆ alkanoyl radical or benzoyl radical,

R₂ means a C₁₋₆ alkyl group,

 R_3 means a hydrogen atom, a C_{1-6} alkyl radical, C_{1-6} alkanoyl radical or benzoylyl radical, and

 R_4 means a hydrogen atom, a C_{1-6} alkyl radical, a C_nF_{2n+1} group, in which n=1, 2 or 3, or a $C = CR_5$ group, in which R_5 is a hydrogen atom, a C_{1-6} alkyl radical or an unsubstituted or substituted phenyl radical.

13. Compounds of general formula I according to claim 12, namely

17-Chloro-17aα-ethinyl-17a,18a-dihomo-estra-1,3,5(10),16-tetraene-3,17aβ-diol

17-chloro-17aα-propinyl-17a,18a-dihomo-estra-1,3,5(10),16-tetraene-3,17aβ-diol

17-chloro-13β-ethyl-17aα-methyl-17a,18a-dihomo-estra-1,3,5(10),16-tetraene-

3,17a_B-diol

17aβ-acetoxy-17-chloro-17a α -methyl-17a, 18a-dihomo-estra-1,3,5(10), 16-tetraene-3-ol

17-chloro-17aα-(trifluoromethyl)-17a,18a-dihomo-estra-1,3,5(10),16-tetraene-3,17aβ-diol

17-chloro-17aα-(pentafluoroethyl)-17a, 18a-dihomo-estra-1,3,5(10),16-tetraene-3,17aβ-diol

17-chloro-17a α -methyl-17a β -(methoxy)-17a, 18a-dihomo-estra-1,3,5(10),16-tetraene-3-ol

17-chloro-17a-homoestra-1,3,5(10),16-tetraene,3,17aβ-diol

17-chloro-17aα-(trifluoromethyl)-17a-homoestra-1, 3,5(10), 16-tetraene-3,17aβ-diol

17-chloro-17aα-(pentafluoroethyl)-17a-homoestra-1,3,5(10),16-tetraene-3,17aβ-diol

17-chloro-17aα-methyl-17a-homoestra-1,3,5(10),16-tetraene-3,17aβ-diol

17-chloro-17aα-ethyl-17a-homoestra-1,3,5(10),16-tetraene-3,17aβ-diol

17-chloro-17aα-ethinyl-17a-homoestra-1,3,5(10),16-tetraene-3,17aβ-diol

17-chloro-17aα-propinyl-17a-homoestra-1,3,5(10),16-tetraene-3,17aβ-diol

17-chloro-17a α -(trifluoromethyl)-17a-homoestra-1,3,5(10),16-tetraene-3,17a β -dioldiacetate

17aβ-acetoxy-17-chloro-17a α -(trifluoromethyl)-17a-homoestra-1,3,5(10),16-tetraene-3-ol

17-chloro-17aβ-methoxy-17a α -(trifluoromethyl)-17a-homoestra-1,3,5(10),16-tetraene-3-ol





7-chloro-(17aα)-21-(4'-methylsulfonylphenyl)-17a,18à-dihomogona-1,3,5(10),16-tetraen-20-yne-3,17aβ-diol

17-chloro-(17aα)-21-(phenyl)-13β-methyl-17a-homogona-1,3,5(10),16-tetraen-20-yne-3,1χaβ-diol

17-chloro-(17a α)-21-(4'-cyanophenyl)-13 β -methyl-17a-homogona-1,3,5(10),16-tetraen-20-yne-3,17a β -diol

17-chloro-(17a α)-21-(4'-acetylaminophenyl)-13 β -methyl-17a-homogona-1,3,5(10),16-tetraen-20-yne-3,17a β -diol α

17-chloro-(17a α)-21-(4'-hydroxyphenyl)-13 β -methyl-17a-homogona-1,3,5(10),16-tetraen-20-yne-3,17a β -diol.

14. Process for the production of 17-chloro-D-homosteroids of the general formula I according to claim 12

$$R_{1}O$$
 R_{2}
 R_{3}
 R_{4}
 Cl
 (I)

characterized in that a 17-chloro-1,3,5(10),16-tetraene-17-one of general formula II





$$R_1O$$

$$R_2$$

$$R_1O$$

in which

 R_1 means a hydrogen atom, a C_{1-5} alkyl radical, a C_{1-6} alkanoyl radical or benzoyl radical.

R₂ means a C₁₋₆ alkyl group,

is converted with a magnesium-organic reagent of general formula BrMg alkyl, BrMg alkenyl or BrMg alkinyl or with acetylene or an alkyl- or aryl-substituted acetylene in the presence of bases such as tert-BuOK or with a lithium-organic compound such as LiC₂F₅ or with a silicon-organic compound such as trifluoromethyl trimethylsilane into a 17aα-substituted compound of general formula III,

$$R_{1}O$$
 R_{2}
 R_{4}
 C_{1}
 $R_{1}O$
 (III)

in which R_1 is a hydrogen atom, a C_{1-6} alkyl radical or C_{1-6} alkanoyl radical or benzoyl radical, and R_2 is a C_{1-6} alkyl group, R_3 is a hydrogen atom, a metal atom or a silyl group, and R_4 is a hydrogen atom, a C_{1-6} alkyl group, a C_nF_{2n+1} group, in which n=1,2 or 3, or is a $C \equiv CR_5$ group, in which R_5 is a hydrogen atom, a C_{1-6} alkyl radical or an unsubstituted or substituted phenyl radical.

whereby in the case of R_{δ} = hydrogen, the free 17a α -ethinyl compound of general formula III is further modified by a SONAGASHIRA reaction to form compounds







with $R_s = C_6H_4R_8$, in which R_6 stands for a free or substituted hydroxyl group, amino group, thiol group, sulfamate group, sulfonyl group or a C_{1-6} alkyl group or C_{6-12} aryl group.

- 15. Process according to claim 14, wherein compounds of formula III, in which R₁ is a C₁₋₅ alkyl radical, are converted by ether cleavage into the free hydroxyl group.
- 16. Process according to claim 14, wherein compounds of formula III, in which R₁ is an acyl radical, are converted by ether cleavage into the free hydroxyl group.
- 17. Process according to claim 14, wherein compounds of formula III, in which R₃ is a hydrogen atom, are converted in a way that is known in the art into ethers or esters.
- 18. Use of the compounds of general formula I according to claim 12 for the production of pharmaceutical agents for contraception in women.
- 19. Use of the compounds of general formula I according to claim 12 for the production of pharmaceutical agents for contraception in men.
- 20. Use of the compounds of general formula I according to claim 12 for the production of pharmaceutical agents for treating benign or malignant proliferative diseases of the ovary.
- 21. Use according to claim 19 for treating ovarian cancer.
- 22. Use according to claim 19 for treating granulosa cell tumors.
- 23. Pharmaceutical compositions that contain at least one compound according to claim 12 or 13, as well as a pharmaceutically compatible vehicle.
- 24. Pharmaceutical compositions according to claim 12, which in addition to at least one compound of general formula I according to claim 1 contain at least one compound that is selected from the group of GnRH antagonists, progesterone receptor antagonists, mesoprogestins, gestagens or tissue-selective gestagens.

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